

What is claimed is:

1 A membrane translocation peptide carrier moiety comprising of formula;

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RQIKIWFQNRRMKWKK (SEQ ID No. 1)

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wherein at least one amino acid residue is deleted from the amino terminus, or variants
10 thereof.

2. A carrier moiety according to claim 1, wherein up to 9 amino acids are deleted.

3. A carrier moiety according to claim 2, wherein from 6 to 9 amino acids are
15 deleted.

4. A carrier moiety according to claim 3, wherein 9 amino acids are deleted.

5. A carrier moiety according to claim 3, selected from the group consisting of:
20 RRMKWKK, NRRMKWKK, QNRRMKWKK and FQNRRMKWKK.

6. A variant of a carrier moiety of claim 1, wherein (a) one or more amino acid
residues are replaced by a naturally or non-naturally occurring amino acid residue (b)
one or more amino acid residues are reversed, (c) both (a) and (b) are present together,
25 (d) a spacer group is present between any two amino acid residues or (e) one or more
amino acid residues are in peptoid form (f) the (N-C-C) backbone of one or more
amino acid residues of the peptide has been modified, or any of (a)-(f) in combination.

7. A carrier moiety according to claim 6, selected from the group consisting of:
30 KRMKWKK, RKMKWKK, RREKWKK, RRQKWKK, RROKWKK, RRMKQKK.

RRMKWFK, RORKWKK, RRMWKKK, RROWKKK, RRMKKWK and RROKKWK.

8. A carrier moiety according to claim 1, represented by any of compounds 2-20.

9. A membrane translocation peptide carrier moiety comprising of formula;

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wherein at least one amino acid residue is replaced by an alternative natural or unnatural replacement α -amino acid residue.

10. A carrier moiety according to claim 9, wherein the sixth amino acid from the amino terminus is not tryptophan.

11. A carrier moiety according to claim 9, wherein the replacement α -amino acid residue is selected from the the group consisting of: residues of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.

12. A carrier moiety according to claim 11, represented by any of compounds 21-36.

13. A carrier moiety of claim 1, wherein free carboxyl group of the carboxy terminal amino acid residue is in the form $-C(O)-NRR'$, wherein R and R' are each independently selected from the group consisting of: hydrogen, C1-6 alkyl, C1-6 alkylene or C1-6 alkynyl, aryl, each optionally substituted by heteroatoms such as O, S or N.

14. A carrier moiety according to claim 13, wherein free carboxyl group of the carboxy terminal amino acid residue is a carboxamide group.
15. A carrier moiety according to claim 14, of the formula $RRMKWKK-NH_2$.
16. A carrier moiety according to claim 1, wherein the peptide is comprised of amino acid residues in their L form.
17. A carrier moiety according to claim 1, wherein the peptide is comprised of amino acid residues in their D form.
18. A carrier moiety according to claim 16, wherein the peptide is in the *retro* form.
19. A membrane translocation vector comprising a membrane translocation peptide carrier moiety as defined claim 1, linked to a cargo moiety.
20. A translocation vector according to claim 19, wherein the cargo moiety is selected from the group consisting of: an oligonucleotide, nucleotide, protein, peptide, biologically active compound and a diagnostic agent.
21. A translocation vector according to claim 20, wherein the cargo moiety is an oligonucleotide or nucleotide selected from the group consisting of: genes, gene fragments, sequences of DNA, cDNA, RNA, nucleotides, nucleosides, heterocyclic bases, synthetic and non-synthetic, sense oligonucleotides, and anti-sense oligonucleotides.
22. A translocation vector according to claim 20, wherein the cargo moiety is a protein or peptide that interferes with the cell cycle.

23. A translocation vector according to claim 22, wherein the cargo moiety is selected from the group consisting of: p53 peptide fragments, p21^{WAF} peptide fragments, Fen1 peptide fragments and p16 peptide fragments.
- 5 24. A translocation vector according to claim 20, wherein the cargo moiety is a drug.
25. A translocation vector according to claim 24, wherein the cargo moiety is derived from a cytotoxic drug.
- 10 26. A translocation vector according to claim 25, wherein the cargo moiety is selected from the group consisting of: DNA damaging agents, anti-metabolites, anti-tumour antibiotics, natural products and their analogues, dihydrofolate reductase inhibitors, pyrimidine analogues, purine analogues, cyclin-dependent kinase
- 15 inhibitors, thymidylate synthase inhibitors, DNA intercalators, DNA cleavers, topoisomerase inhibitors, anthracyclines, vinca drugs, mitomycins, bleomycins, cytotoxic nucleosides, pteridine drugs, diynes, podophyllotoxins, platinum containing drugs, differentiation inducers and taxanes.
- 20 27. A translocation vector according to claim 26, wherein the cargo moiety is the group consisting of: methotrexate, methopterin, dichloromethotrexate, 5-fluorouracil, 6-mercaptopurine, tri-substituted purines such as olomoucine, roscovitine and bohemine, flavopiridol, staurosporin, cytosine arabinoside, melphalan, leurosine, actinomycin, daunorubicin, doxorubicin, mitomycin D, mitomycin A, carminomycin,
- 25 aminopterin, tallysomycin, podophyllotoxin, etoposide, cisplatin, carboplatin, vinblastine, vincristine, vindesine, paclitaxel, docetaxel, taxotere, retinoic acid, butyric acid, acetyl spermidine, tamoxifen, irinotecan and camptothecin.
28. A translocation vector according to claim 19, wherein the cargo moiety is
- 30 directly linked to the carrier moiety.

29. A translocation vector according to claims 19, wherein the cargo moiety is indirectly linked to the carrier moiety by means of a linker moiety.

5 30. A translocation vector according to claim 19, further comprising a targeting moiety.

31. A translocation vector according to claim 30, wherein the targeting moiety is attached to the carrier moiety.

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32. A translocation vector according to claim 30, wherein the targeting moiety is attached to the cargo moiety.

33. A translocation vector according to claim 19, wherein each carrier moiety bears
15 more than one cargo moiety.

34. A translocation vector according to claim 33, wherein the cargo moieties are different.

20 35. A translocation vector according to claim 33, wherein the cargo moieties are attached to the carrier by a network of lysine residues.

36. A translocation vector according to claim 19, wherein the carrier moiety peptide is comprised of amino acid residues in their L form.

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37. A translocation vector according to claim 19, wherein the carrier moiety peptide is comprised of amino acid residues in their D form.

38. A translocation vector according to claims 19, wherein the carrier moiety
30 peptide is in the *retro* form.

39. A translocation vector according to claim 23, wherein both the carrier moiety peptide and the cargo moiety are in the L form.

5 40. A translocation vector according to claim 23, wherein both the carrier moiety peptide and the cargo moiety are in the D form.

41. A translocation vector according to claim 23, wherein the carrier moiety peptide is in the D form and the cargo moiety in the L form.

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42. A translocation vector according to claim 23, wherein the carrier moiety peptide is in the L form and the cargo moiety in the D form.

43. A vector according to claim 19, that translocates the cell membrane and
15 remains in the cytosol.

44. A vector according to claims 19, that translocates the cell membrane and the nuclear membrane.

20 45. A membrane translocation peptide carrier moiety comprising up to 15 amino acid residues and at least the peptide for formula;

RRMKWKK (I)

25 or variants thereof.

46. A delivery systems selected from the group consisting of::

#	Drug moiety	Linker moiety	Carrier moiety
	paclitaxel	2'-succinimidopropionoyl-C β A	RRMKWKK-NH ₂
	podophyllotoxin	4-succinimidopropionoyl-C β A	RRMKWKK-NH ₂
	podophyllotoxin	4-succinimidopropionoyl-C β A	(D-R)(D-R)(D-M)(D-K)(D-W)(D-K)(D-K-NH ₂)
	epipodophyllotoxin	4'-succinimidopropionoyl-C β A	RRMKWKK-NH ₂
	podophyllotoxin	4-acetyl-C β A	RRMKWKK-NH ₂
	4'-demethyl epipodophyllotoxin	4-acetyl-C β A	RRMKWKK-NH ₂
	podophyllotoxin	4-succinimidopropionoyl-GC β A	RRMKWKK-NH ₂
C-term	podophyllotoxin	4-succinimidopropionoyl-C	RRMKWKK
N-term	podophyllotoxin	4-succinimidopropionoyl-C	
N-term	epipodophyllotoxin	4'-succinimidopropionoyl-C	RRMKWKK
C-term	camptothecin	10-O-succinimidopropionoyl-C	
N-term	epipodophyllotoxin	4'-succinimidopropionoyl-C	RRMKWKK
C-term	paclitaxel	2'-(succinimido)propionoyl-C	
	4'-methoxy-epipodophyllotoxin	4-(4"-aminoanilino)succinimidopropionoyl-C β A	RRMKWKK-NH ₂
	4'-demethyl-epipodophyllotoxin	4-(4"-aminoanilino)succinimidopropionoyl-C β A	RRMKWKK-NH ₂